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=> s cholesteryl ester transfer protein

L1 3985 CHOLESTERYL ESTER TRANSFER PROTEIN

=> s l1 and method

L2 483 L1 AND METHOD

=> s l2 and CETP

L3 380 L2 AND CETP

=> s l3 and CETP activity

L4 139 L3 AND CETP ACTIVITY

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L5 0 L4 AND HUMANIZED

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L6 21 L4 AND RABBIT

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L8 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2001 ACS
1999:282118 Document No. 130:310673 Xenogeneic **cholesteryl ester transfer protein** (**CETP**) for modulation of **CETP activity** in treatment of atherosclerosis. Rittershaus, Charles W.; Thomas, Lawrence J. (Avant Immunotherapeutics, Inc., USA). PCT Int. Appl. WO 9920302 A1 19990429, 62

pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE,

BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US22145 19981020. PRIORITY: US 1997-954643 19971020.

AB **Methods** for modulating **cholesteryl ester transfer protein** (**CETP**) **activity** and the plasma levels of lipoproteins involved in heart disease involve administration of a non-endogenous **CETP** or a plasmid-based vaccine for expression of such non-endogenous **CETP** to elicit prodn. in a mammal of antibodies that recognize (bind to) the mammal's native (endogenous) **CETP**.

L8 ANSWER 2 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS

1999:468093 Document No.: PREV199900468093. Combined effects of probucol and bezafibrate on lipoprotein metabolism and liver **cholesteryl ester transfer protein** mRNA in cholesterol-fed **rabbits**. Ou, Jiafu; Saku, Keijiro (1); Jimi, Shiro; Liao, Yuan-Lan; Ohta, Takao; Zhang, Bo; Arakawa, Kikuo. (1) Department of Internal Medicine, Fukuoka University School of Medicine, 45-1-7 Nanakuma Jonanku, Fukuoka, 814-0180 Japan. Japanese Circulation Journal, (June, 1999) Vol. 63, No. 6, pp. 471-477. ISSN: 0047-1828. Language: English. Summary Language: English.

AB Probucol decreases and bezafibrate increases plasma high density lipoprotein-cholesterol (HDL-C) levels in humans. This study was performed to determine whether the HDL-C-lowering effects of probucol could be reversed by treatment with bezafibrate in hypercholesterolemic **rabbits**. Forty-nine normolipidemic Japanese White **rabbits** were divided into 5 groups (group 1: normal chow; group 2: 0.2% cholesterol (Ch) diet; group 3: 0.2% Ch and 1% probucol diet; group 4: 0.2% Ch and 1% bezafibrate diet; group 5: 0.2% Ch and 1% probucol plus 1% bezafibrate diet) and treated for 8 weeks. Plasma lipids, **cholesteryl ester transfer protein** (**CETP**) **activity** in the lipoprotein-deficient plasma fraction, **CETP** mRNA in liver tissue and plasma drug concentrations were investigated. Serum total cholesterol (TC) increased after the **rabbits** in groups 2, 3, 4 and 5 were fed Ch, but overall, no significant differences were observed in serum TC and triglyceride (TG) among these groups. Serum HDL-C levels increased ($p<0.01$) in the bezafibrate-treated group, but a significant ($p<0.05$) reduction in HDL-C was observed in both the Ch + probucol (group 3) and Ch + probucol plus bezafibrate (group 5) groups; no significant difference was observed between groups 3 and 5. Significant correlation ($p<0.01$) was found between serum low density lipoprotein cholesterol (LDL-C) levels and plasma probucol concentrations in groups 3 and 5, but no correlation was found between plasma concentrations of probucol/bezafibrate and serum HDL-C levels. **CETP activity** in the lipoprotein-deficient plasma fraction increased in the Ch-, Ch + probucol-, and Ch + probucol and bezafibrate-fed groups (groups 2, 3 and 5, respectively), whereas a significant reduction in this activity was observed in the Ch + bezafibrate-fed group (group 4). An analysis of covariance showed that the **CETP activity** responded more sensitively to drug treatment than did the serum HDL-C level. **CETP** mRNA in liver tissue was assessed by Northern blotting at 8 weeks, but no changes were observed among the 5 groups. Probucol decreased and bezafibrate increased serum HDL-C levels, through **CETP activity** without affecting liver **CETP** mRNA levels, and the decrease in HDL-C levels produced by probucol could not be reversed by bezafibrate.

L8 ANSWER 3 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
1998:251919 Document No.: PREV199800251919. A peptide from hog plasma that inhibits human **cholesteryl ester transfer protein**. Cho, Kyung-Hyun; Lee, Ju-Young; Choi, Myung-Sook; Cho, Joong Myung; Lim, Jong-Soon; Park, Yong Bok (1). (1) Dep. Genet. Eng., Coll. Nat. Sci., Kyungpook Natl. Univ., Taegu 702-701 South Korea . Biochimica et Biophysica Acta, (March 30, 1998) Vol. 1391, No. 2, pp. 133-144. ISSN: 0006-3002. Language: English.

AB A peptide that inhibits the human **cholesteryl ester transfer protein** (**CETP**) was isolated from hog plasma by ultracentrifugation, two sequential column chromatographies and electroelution from gels. Molecular weight of the peptide was determined to be approximately 3 kDa on the SDS-PAGE. The peptide contained 28 amino acids with an identical sequence to the amino terminus of hog apolipoprotein-CIII except two amino acid residues: -Pro-Glu- at the fifth and sixth amino acids from the amino terminus in the isolated peptide, in contrast to -Leu-Leu- in hog apo-CIII. A peptide synthesized chemically according to the amino acid sequence of the peptide (designated P28) showed approximately the same degree of **CETP** inhibitory activity as the isolated peptide. Synthetic peptides with different number of amino acids were also tested for **CETP** inhibition. Among the peptides, the one with 20 amino acid residues (P20) from the amino terminus showed the highest inhibitory activity against the **CETP**. The peptide appeared to be associated with the hog high-density lipoproteins (HDL), as determined by immunoblot analysis using antibody against P28. The **CETP**-inhibitory activity of the peptide was examined in vivo using diet-induced hypercholesterolemic **rabbits**. When the peptide was injected into the **rabbits** (7-9 mg/kg body weight), approximately 75% **CETP activity** disappeared from the plasma in 1 h after the injection and the effect lasted up to 30 h. The inhibition of **CETP** in vivo led to a concomitant decrease in total plasma cholesterol level up to 30% and an increase in the level of HDL-cholesterol up to 32%. The cholesterol concentrations in the **rabbit** plasma gradually recovered to the initial level after 48 h.

L8 ANSWER 4 OF 13 MEDLINE
1998225000 Document Number: 98225000. PubMed ID: 9565327. Enzyme immunoassay for **cholesteryl ester transfer protein** in human serum. Kiyohara T; Kiriyama R; Zamma S; Inazu A; Koizumi J; Mabuchi H; Chichibu K. (Diagnostics Research Labs, Chugai Pharmaceutical Co., Ltd., Tokyo, Japan.) CLINICA CHIMICA ACTA, (1998 Mar 23) 271 (2) 109-18. Journal code: DCC; 1302422. ISSN: 0009-8981. Pub. country: Netherlands. Language: English.

AB We developed a new simple sandwich-type enzyme immunoassay to measure **cholesteryl ester transfer protein** (**CETP**) mass in human serum. In assay validation, Intra- and Inter-assay coefficients of variation were 2.7 to 5.7% and 2.2 to 12.2%, respectively. There was no cross-reactivity with various lipoproteins (apo A-I, apo A-II, apo B, apo C-III). A good correlation between **CETP** mass and **CETP activity** (n = 46, correlation coefficient = 0.88) was observed. This assay provided a specific and reproducible **method** for measuring **CETP** mass in samples. The average value of **CETP** in the normal sera of 41 males was 1.8+/-0.6 microg/ml (mean+/-S.D.) and that of 37 females was 2.0+/-0.5 microg/ml. In the study of patients with the **CETP** gene mutation (Int 14A and D442G), our results on the value of plasma **CETP** mass reflected to genetic **CETP** deficiency. In conclusion, this assay for **CETP** mass in human serum may be a useful tool for clinical investigations involving lipid metabolism related

to disease.

L8 ANSWER 5 OF 13 MEDLINE DUPLICATE 1
96325006 Document Number: 96325006. PubMed ID: 8702580. Changes in plasma
lipoprotein cholesterol levels by antisense oligodeoxynucleotides against **cholesteryl ester transfer protein**
in cholesterol-fed **rabbits**. Sugano M; Makino N. (Department of Bioclimatology and Medicine, Medical Institute of Bioregulation, Kyushu University, 4546 Tsurumihara, Beppu, Oita 874, Japan.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Aug 9) 271 (32) 19080-3. Journal code: HIV; 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB **Cholesteryl ester transfer protein**
(**CETP**) is the enzyme that facilitates the transfer of cholesteryl ester from high density lipoprotein (HDL) to apoB-containing lipoproteins and also affects the low density lipoprotein metabolism. On the other hand, the liver is the major tissue responsible for the production of **CETP** (**CETP** mRNA) in **rabbits**.
To test the hypothesis that a reduction of **CETP** mRNA in the liver by antisense oligodeoxynucleotides (ODNs) may affect the plasma lipoprotein cholesterol levels, we intravenously injected antisense ODNs against **rabbit CETP** coupled with asialoglycoprotein carrier molecules, which serve as an important **method** to regulate liver gene expression, to cholesterol-fed **rabbits** via their ear veins. All **rabbits** were fed a standard **rabbit** chow supplement with 0.1% cholesterol for 10 weeks before and throughout the experiment. After injecting **rabbits** with antisense ODNs, the plasma total cholesterol concentrations and plasma **CETP activities** all decreased at 24, 48, and 96 h, whereas the plasma HDL cholesterol concentrations increased at 48 h. A reduction in the hepatic **CETP** mRNA was also observed at 6, 24, and 48 h after the injection with antisense ODNs. However, in the **rabbits** injected with sense ODNs, the plasma total and HDL cholesterol concentrations and the plasma **CETP activities** did not significantly change, and the hepatic **CETP** mRNA did not change either throughout the experimental period. Although the exact role of **CETP** in the development of atherosclerosis remains to be clarified, these findings showed for the first time that the intravenous injection with antisense ODNs against **CETP** coupled to asialoglycoprotein carrier molecules targeted to the liver could thus inhibit plasma **CETP activity** and, as a result, could induce a decrease in the plasma low density lipoprotein and very low density lipoprotein cholesterol and an increase in the plasma HDL cholesterol in cholesterol-fed **rabbits**.

L8 ANSWER 6 OF 13 SCISEARCH COPYRIGHT 2001 ISI (R)
96:362104 The Genuine Article (R) Number: UJ238. CHOLESTERYL ESTER TRANSFER ACTIVITY IN LIVER-DISEASE AND CHOLESTASIS, AND ITS RELATION WITH FATTY-ACID COMPOSITION OF LIPOPROTEIN LIPIDS. IGLESIAS A; ARRANZ M; ALVAREZ J J; PERALES J; VILLAR J; HERRERA E; LASUNCION M A (Reprint). HOSP
RAMON Y CAJAL, SERV BIOQUIM INVEST, UNIDAD DISLIPEMIAS, CTRA COLMENAR, KM 9, E-28034 MADRID, SPAIN (Reprint); HOSP RAMON Y CAJAL, SERV BIOQUIM INVEST, UNIDAD DISLIPEMIAS, E-28034 MADRID, SPAIN; HOSP RAMON Y CAJAL, SERV BIOQUIM CLIN, E-28034 MADRID, SPAIN; HOSP RAMON Y CAJAL, MED INTERNA SERV, E-28034 MADRID, SPAIN; UNIV ALCALA DE HENARES, MADRID, SPAIN. CLINICA CHIMICA ACTA (30 APR 1996) Vol. 248, No. 2, pp. 157-174. ISSN: 0009-8981. Pub. country: SPAIN. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Liver disease is accompanied by major qualitative and quantitative disturbances in plasma lipoprotein metabolism, the extent and intensity of
which depend on the degree of parenchymal damage, cholestasis, or both.

The main objective of this study was to determine the cholesteryl ester transfer **CETP activity** and its association with the lipoprotein neutral lipid composition in patients with either liver cirrhosis or cholestasis, as compared to normal controls. Lipoproteins were isolated by ultracentrifugation, lipids and apolipoproteins were measured by conventional **methods**, and the fatty acid composition was established by gas chromotography; **CETP activity** in lipoprotein-deficient plasma was measured by determining the transfer of [H-3]cholesteryl esters from HDL to VLDL, Lipoprotein lipase and hepatic lipase activities were measured in post-heparin plasma by radiochemical **methods**. In patients with liver cirrhosis, low levels of VLDL, HDL, apo B, and Lp(a) were observed, as well as a change in the composition of HDL particles, with increases in the relative proportion of triglyceride and free cholesterol. Respectively, the last two changes could be attributed in part to the low hepatic lipase activity observed in this study, and to the low lecithin:cholesterol acyltransferase activity previously observed by others. In patients with cholestasis, a moderate hyperlipidemia due to the elevation of LDL was found. In contrast, HDL and apo A-I levels were very low reflecting a low number of HDL particles, which also had altered compositions with increases in the triglyceride and free cholesterol contents relative to apo A-I and esterified cholesterol, respectively. As regards the fatty acid composition of lipoprotein lipids, the two groups of patients showed, in general, a lower proportion of linoleic acid and a compensating higher proportion of oleic acid as compared to the controls, changes that were observed in both cholesteryl esters and triglycerides. In contrast, the proportions of oleic and palmitoleic acids in phospholipids were increased, whereas that of stearic acid was decreased in patients as compared to controls. In patients with liver cirrhosis, as well as in controls, no changes were observed in the fatty acid compositions of cholesteryl ester, triglycerides, or phospholipids among the different lipoproteins, which probably reflects the equilibration reached by the action of **CETP**. In patients with cholestasis, no differences were observed in fatty acid composition among the lipoprotein phospholipids but, interestingly, cholesteryl esters from VLDL had a significantly lower linoleic acid content than those from HDL, whereas triglycerides from VLDL had significantly higher oleic acid and lower linoleic acid contents than those from HDL. This distinct fatty acid composition of the neutral lipids between lipoproteins was associated with a significant decrease (25%) in the cholesteryl ester transfer activity in patients with cholestasis. We suggest that fat malabsorption due to the biliary defect may induce a decrease in **cholesteryl ester transfer protein** synthesis or secretion, which in turn would slow the equilibration of the neutral lipids among plasma lipoproteins.

L8 ANSWER 7 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS

1994:221962 Document No.: PREV199497234962. Two-site enzyme immunoassay of **cholesteryl ester transfer protein** with monoclonal and oligoclonal antibodies. Mezdour, Hafid (1); Kora, Ibrahim; Parra, Henri J.; Tartar, Andre; Marcel, Yves L.; Fruchart, Jean-Charles. (1) Inst. Pasteur de Lille, Serlia et INSERM U-325, 1 rue du Professeur Calmette, 59019 Lille France. Clinical Chemistry, (1994) Vol. 40, No. 4, pp. 593-597. ISSN: 0009-9147. Language: English.

AB We developed a sandwich-type enzyme immunoassay to measure **cholesteryl ester transfer protein** (**CETP**) mass in human plasma. A specific monoclonal antibody (TP-4) that recognizes an epitope located in the C-terminal domain was used for antigen capture and an anti-**CETP** peptide antibody directed

against the 290-306 residue was used for detection. Bound antibodies were revealed with an antibody-peroxidase conjugate specific for **rabbit** IgG. The presence of 10 mL/L Triton X-100 in the incubation buffer increased antigen exposure of **CETP** in plasma. The curves for **CETP** in standard plasma and partially purified **CETP** were parallel. This technique is rapid (results within 6 h), accurate, precise (mean intra and interassay CVs 3.6% and 8.4%, respectively), and simple to perform. Assay sensitivity is at microgram concentrations, with a working range of 20-200 mu-g/L. In 40 normolipidemic healthy subjects, the mean **CETP** concentration in plasma was 1.1 +- 0.4 mg/L. A strong correlation between **CETP** concentration and **CETP activity** (r = 0.91, n = 42) was observed. In plasma, the bulk of **CETP** was found in high-density lipoprotein fractions. Therefore, this assay may be a useful tool for investigations of **CETP** and its significance in relevant diseases.

L8 ANSWER 8 OF 13 MEDLINE DUPLICATE 2
94045262 Document Number: 94045262. PubMed ID: 8228645. Use of fluorescent cholesteryl ester microemulsions in **cholesteryl ester transfer protein** assays. Bisgaier C L; Minton L L; Essenburg A D; White A; Homan R. (Department of Pharmacology, Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI 48105.) JOURNAL OF LIPID RESEARCH, (1993 Sep) 34 (9) 1625-34. Journal code: IX3; 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB In the present report we describe a simple and practical **method** to assess **CETP activity** in a defined system by use of microemulsions containing a fluorescent cholesteryl ester analog. The microemulsions are stable, simple to prepare, and can be made to defined composition. Initial transfer rates are easily determined by monitoring changes in fluorescence. We have used the fluorescent cholesteryl ester analog, cholesteryl 4,4-difluoro-5,7-dimethyl-4-boro-3 alpha, 4 alpha-diaza-3-indacenedodecanoate (BODIPY-CE), to demonstrate the utility of this assay. The assay takes advantage of the concentration-dependent self-quenching of BODIPY-CE, when this analog is incorporated into microemulsions. We have used this new assay to demonstrate fluorescent lipid transfer facilitated by **rabbit** and human d > 1.21 g/ml plasma fraction and recombinant human **CETP**. A known inhibitory monoclonal antibody (Mab) to human **CETP** blocked BODIPY-CE transfer in a dose-dependent manner. We have also used BODIPY-CE microemulsions to measure **CETP activity** in whole plasma.

L8 ANSWER 9 OF 13 MEDLINE
93267201 Document Number: 93267201. PubMed ID: 8496672. Polyclonal antibody-based immunoradiometric assay for quantification of **cholesteryl ester transfer protein**. Ritsch A; Auer B; Foger B; Schwarz S; Patsch J R. (Department of Medicine, University of Innsbruck, Austria.) JOURNAL OF LIPID RESEARCH, (1993 Apr) 34 (4) 673-9. Journal code: IX3; 0376606. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB **Cholesteryl ester transfer protein** (**CETP**) catalyzes the transfer of neutral lipids among plasma lipoproteins and in this way plays a prominent role in cholesterol metabolic routing and, thus, probably for atherosclerosis. Studies of this important protein in various clinical settings require the ability to accurately quantify **CETP** in plasma. In order to gain access to such a capability, an immunoradiometric assay (IRMA) for quantification of **CETP** was developed. **CETP** was purified from human plasma to apparent homogeneity and used for raising anti-**CETP**

antibodies in **rabbits**. The specificity of the polyclonal antiserum obtained was demonstrated by inhibition assays and immunoblot analysis. Before use in the **CETP**-IRMA, the antibodies were affinity-purified by chromatography on **CETP**-Sepharose. Sensitivity of the **CETP**-IRMA was 0.1 ng, and intra- and interassay coefficients of variation were 2.9 and 8.0%, respectively. In 30 normolipidemic healthy subjects, the mean (+/- SD) **CETP** concentration was 1.1 (+/- 0.22) micrograms/ml of plasma; individual values ranged from 0.644 to 1.694 micrograms **CETP**/ml and agreed well with measurements of **CETP activity** of the same samples (r = 0.85).

L8 ANSWER 10 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
1993:288790 Document No.: PREV199345006915. Ethanol reduces the accumulation of **cholesteryl ester transfer protein** (**CETP**) **activity** in the medium of perfused **rabbit** livers. Hannuksela, Minna; Rantala, Maire; Kesaniemi, Y. Antero; Savolainen, Markku J.. Dep. Internal Med., University Oulu, Oulu Finland. Circulation, (1992) Vol. 86, No. 4 SUPPL. 1, pp. I692. Meeting Info.: 65th Scientific Sessions of the American Heart Association New Orleans, Louisiana, USA November 16-19, 1992 ISSN: 0009-7322. Language: English.

L8 ANSWER 11 OF 13 BIOSIS COPYRIGHT 2001 BIOSIS
1992:241886 Document No.: BR42:112186. FLUORESCENT DETERMINATION OF **CHOLESTERYL ESTER TRANSFER PROTEIN** **CETP ACTIVITY** IN PLASMA. DOUSSET N; DOUSTE-BLAZY L. SERVICE DE BIOCHIM, HOPITAL RANGUEIL, 1 AVE. J. POULHES, 31054, TOULOUSE CEDEX, FRANCE.. Clin. Chem. (Winston-Salem, N. C.), (1992) 38 (2), 306. CODEN: CLCHAU. ISSN: 0009-9147. Language: English.

L8 ANSWER 12 OF 13 SCISEARCH COPYRIGHT 2001 ISI (R)
91:195621 The Genuine Article (R) Number: FE094. ELEVATED **CHOLESTERYL ESTER TRANSFER PROTEIN**-ACTIVITY IN IDDM MEN WHO SMOKE - POSSIBLE FACTOR FOR UNFAVORABLE LIPOPROTEIN PROFILE.
DULLAART R P F (Reprint); GROENER J E M; DIKKESCHEI B D; ERKELENS D W; DOORENBOS H.
STATE UNIV GRONINGEN HOSP, DEPT ENDOCRINOL, OOSTERSINGEL 59, POB 30001, 9700 RB GRONINGEN, NETHERLANDS (Reprint); STATE UNIV GRONINGEN HOSP, DEPT CLIN CHEM, 9700 RB GRONINGEN, NETHERLANDS; ERASMUS UNIV, DEPT BIOCHEM 1, 3000 DR ROTTERDAM, NETHERLANDS; STATE UNIV UTRECHT HOSP, DEPT INTERNAL MED, 3511 GV UTRECHT, NETHERLANDS. DIABETES CARE (1991) Vol. 14, No. 4, pp. 338-341. Pub. country: NETHERLANDS. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Objectives: To determine the effect of cigarette smoking on the activity of **cholesteryl ester transfer protein** (**CETP**) and high-density (HDL), low-density (LDL), and very-low-density (VLDL) lipoproteins in insulin-dependent diabetic (IDDM) men with microvascular complications. Research Design and

Methods: We performed a case-control study in a referral-based diabetes clinic on a sequential sample of 9 cigarette-smoking and 12 nonsmoking IDDM men with microvascular complications and 12 nonsmoking control men. **CETP activity** was determined in each serum with an isotope assay with exogenous cholesteryl ester-labeled LDL and HDL. The **method** is independent of the endogenous lipoprotein present in serum. Results: The HDL-cholesterol (VLDL and LDL) ratio was lower in the smoking diabetic men than in the other groups ($P < 0.05$ vs. the nonsmoking diabetic men and $P < 0.01$ vs. the control subjects). **CETP activity** was 70% higher in the smoking diabetic men than in the control subjects ($P < 0.01$) and 30% higher than in the nonsmoking diabetic men ($P < 0.05$). The

HDL-cholesterol (VLDL and LDL) ratio and the apolipoprotein A-I-B ratio were inversely correlated to **CETP activity** in the diabetic patients ($r = -0.52$, $P < 0.02$ and $r = -0.45$, $P < 0.05$, respectively). Conclusions: **CETP activity** is increased in cigarette-smoking IDDM men with microvascular complications. High **CETP activity** may contribute to the unfavorable lipoprotein profile in these patients.

L8 ANSWER 13 OF 13 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
87147784 EMBASE Document No.: 1987147784. Comparative molecular weight of **cholesteryl ester transfer protein** from cyclophosphamide- and irradiation-treated **rabbits**: Size determination by radiation inactivation **method**. Loudet A.-M.; Dousset N.; Potier M.; et al.. INSERM Unite 101, Biochimie des Lipides, Hopital Purpan, 31059 Toulouse, France. Medical Science Research 15/5 (251-252) 1987.
CODEN: MSCREJ. Pub. Country: United Kingdom. Language: English.
AB Previous results concerning the cholesteryl transfer protein (**CETP**) **activity** between HDL and VLDL have led us to determine the molecular weight (Mr) of this molecule. In fact, we have observed an increase of **CETP activity** in antimitotic (cyclophosphamide) treated **rabbit**. In order to evaluate the molecular size of this protein, we have chosen the radiation inactivation **method** because this technique can determine in certain conditions the size of the functional unit in situ. Results showed that this molecule was not influenced by antimitotic treatment since we obtained a Mr of about 71,000 and 72,000 respectively for control and cyclophosphamide-treated **rabbits**. A similar value was obtained for **rabbits** after total whole-body irradiation. Since the molecular size by radiation inactivation corresponds to the subunit of the enzyme, we can conclude that the functional unit of this enzyme, i.e. the minimal assembly of structure required for biological activity, is the subunit.

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L11 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2001 ACS
2001:651566 Plasmid-based vaccine for treating atherosclerosis. **Thomas, Lawrence J.** (AVANT Immunotherapeutics, Inc., USA). U.S. US 6284533 B1 20010904, 35 pp., Cont.-in-part of U.S. Ser. No. 802,967. (English).
CODEN: USXXAM. APPLICATION: US 1998-171969 19981002. PRIORITY: US 1996-PV52983 19960501; US 1997-802967 19970221; WO 1997-US7294 19970501.
AB A plasmid-based vaccine is provided herein based on the combination of DNA segments coding for one or more B cell epitopes of cholesteryl ester transfer protein (**CETP**) and one or more broad range helper T cell epitopes. Administration of the plasmids as a vaccine to a vertebrate subject provides an immune response to the subject's endogenous

CETP and modulation of **CETP** activity, leading to prevention or reversal of various manifestations of heart disease. The vaccines provide an advantageous strategy for the prevention or treatment of atherosclerosis.

L11 ANSWER 2 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
2001:298985 Document No.: PREV200100298985. An extended toxicologic evaluation
of an immunoneutralizing vaccine to produce anti-**CETP** antibodies for the prevention/treatment of atherosclerosis. **Thomas, Lawrence J. (1)**; Picard, Michele D. (1); Miller, David P. (1); Emmett, Constance D. (1); Scesney, Susanne M. (1); Pisano, Milissa L. (1); Adari, Hedy (1); Hammond, Russell A. (1); Marsh, Henry C. (1); **Rittershaus, Charles W. (1)**; Pettey, Carolyn L. (1). (1) AVANT Immunotherapeutics, 119 Fourth Ave., Needham, MA, 02494 USA. FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A566. print. Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001 ISSN: 0892-6638. Language: English. Summary Language: English.

AB A toxicology study was conducted with an immunoneutralizing vaccine designed to elicit antibodies that would bind to and block the function of
cholesteryl ester transfer protein (**CETP**), in order to prevent atherosclerosis. The vaccine consisted of a dimer of a 31 a.a. synthetic chimeric peptide containing an N-terminal cysteine, a T cell epitope (residues 830-843 of tetanus toxin), and a B cell epitope (residues 461-476 of human **CETP**), formulated with an alum adjuvant. In this study NZW rabbits were immunized with either 0 mg (4 males and 4 females), 0.1 mg (2 males and 2 females), 0.25 mg (4 males and 4 females) or 1.0 mg (4 males and 4 females) of the vaccine on days 1, 29 and 57. On day 197 (at a relative antibody minimum) half of the animals from groups 1, 3 and 4 were sacrificed. The remaining animals were reboosted and euthanized on day 211, at an expected antibody maximum. Blood samples were
taken periodically throughout the study and were assessed for hematology, clinical chemistry, and antibody titers. All rabbits in the non-control groups developed anti-rabbit **CETP** antibody titers, thus validating the immunogenicity of the vaccine. In all other measurements the vaccinated groups were indistinguishable from the control group. All animals were monitored for clinical abnormalities throughout the study, and at necropsy, gross pathology was assessed, selected organs were weighed, and samples of 44 tissues were taken for histopathology. By all the above parameters, no significant test article-related pathology was observed. This study demonstrated the administration of this **CETP** immunoneutralizing vaccine produced specific self-reactive antibody titers
but no detectable test article-related pathology.

L11 ANSWER 3 OF 12 MEDLINE DUPLICATE 2
2000482102 Document Number: 20436374. PubMed ID: 10978256.
Vaccine-induced antibodies inhibit **CETP** activity in vivo and reduce aortic lesions in a rabbit model of atherosclerosis.
Rittershaus C W; Miller D P; **Thomas L J**; Picard M D; Honan C M; Emmett C D; Pettey C L; Adari H; Hammond R A; Beattie D T; Callow A D; Marsh H C; Ryan U S. (AVANT Immunotherapeutics, Inc, Needham, MA 02494, USA.. crittershaus@avantimmune.com) . ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (2000 Sep) 20 (9) 2106-12. Journal code: B89; 9505803. ISSN: 1524-4636. Pub. country: United States. Language: English.

AB Using a vaccine approach, we immunized New Zealand White rabbits with a peptide containing a region of cholesteryl ester transfer protein (**CETP**) known to be required for neutral lipid transfer function. These rabbits had significantly reduced plasma **CETP** activity and an altered lipoprotein profile. In a cholesterol-fed rabbit model of

atherosclerosis, the fraction of plasma cholesterol in HDL was 42% higher and the fraction of plasma cholesterol in LDL was 24% lower in the **CETP**-vaccinated group than in the control-vaccinated group. Moreover, the percentage of the aorta surface exhibiting atherosclerotic lesion was 39.6% smaller in the **CETP**-vaccinated rabbits than in controls. The data reported here demonstrate that **CETP** activity can be reduced in vivo by vaccination with a peptide derived from **CETP** and support the concept that inhibition of **CETP** activity in vivo can be antiatherogenic. In addition, these studies suggest that vaccination against a self-antigen is a viable therapeutic strategy for disease management.

L11 ANSWER 4 OF 12 SCISEARCH COPYRIGHT 2001 ISI (R)
2000:559012 The Genuine Article (R) Number: 313NH. Toxicologic evaluation of an immunoneutralizing vaccine to produce anti-**CETP** antibodies for the prevention/treatment of atherosclerosis.. **Thomas L J (Reprint)**; Picard M D; Miller D P; Emmett C D; Scesney S M; Adari H; Hammond R A; Levin J L; Ryan U S; Marsh H C; Pettey C L; **Rittershaus C W**. AVANT IMMUNOTHERAPEUT INC, NEEDHAM, MA 02494. FASEB JOURNAL (11 MAY 2000) Vol. 14, No. 8, pp. 262-262. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0892-6638. Pub. country: USA. Language: English.

L11 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2001 ACS
1999:282118 Document No. 130:310673 Xenogeneic cholesteryl ester transfer protein (**CETP**) for modulation of **CETP** activity in treatment of atherosclerosis. **Rittershaus, Charles W.**; **Thomas, Lawrence J.** (Avant Immunotherapeutics, Inc., USA). PCT Int. Appl. WO 9920302 A1 19990429, 62 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US22145 19981020. PRIORITY: US 1997-954643 19971020.
AB Methods for modulating cholesteryl ester transfer protein (**CETP**) activity and the plasma levels of lipoproteins involved in heart disease involve administration of a non-endogenous **CETP** or a plasmid-based vaccine for expression of such non-endogenous **CETP** to elicit prodn. in a mammal of antibodies that recognize (bind to) the mammal's native (endogenous) **CETP**.

L11 ANSWER 6 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
1999:282999 Document No.: PREV199900282999. A vaccine to produce anti-cholesteryl ester transfer protein (**CETP**) antibodies for the prevention/treatment of atherosclerosis. **Thomas, L. J. (1)**; Picard, M. D. (1); Miller, D. P. (1); Honan, C. M. (1); Adari, H. (1); Emmett, C. D. (1); Marsh, H. C. (1); Ryan, U. S. (1); Pettey, C. L. (1); **Rittershaus, C. W. (1)**. (1) Avant Immunotherapeutics, Inc., Needham, MA, 02494 USA. FASEB Journal, (March 15, 1999) Vol. 13, No. 5 PART 2, pp. A693. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 99 Washington, D.C., USA April
17-21, 1999 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L11 ANSWER 7 OF 12 SCISEARCH COPYRIGHT 2001 ISI (R)
1998:762763 The Genuine Article (R) Number: 121HC. Use of xenogeneic cholesteryl ester transfer protein (**CETP**) in a plasmid-based vaccine to produce anti-**CETP** autoantibodies for the prevention/treatment of atherosclerosis.. **Thomas L J (Reprint)**; Adari H; Picard M D; Honan C M; Miller D P; **Rittershaus C W**;

Pettey C L. T CELL SCI INC, NEEDHAM, MA. FASEB JOURNAL (17 MAR 1998) Vol. 12, No. 4, Part 1, Supp. [S], pp. 1805-1805. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0892-6638. Pub. country: USA. Language: English.

L11 ANSWER 8 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
1998:200178 Document No.: PREV199800200178. Use of xenogeneic cholesteryl ester transfer protein (**CETP**) in a plasmid-based vaccine to produce anti-**CETP** autoantibodies for the prevention/treatment of atherosclerosis. **Thomas, L. J.**; Adari, H.; Picard, M. D.; Honan, C. M.; Miller, D. P.; **Rittershaus, C. W.**; Pettey, C. L.. T Cell Sciences Inc., Needham, MA USA. FASEB Journal, (March 17, 1998) Vol. 12, No. 4, pp. A310. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 98, Part 1 San Francisco, California, USA April 18-22, 1998 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L11 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2001 ACS
1997:740308 Document No. 128:10315 Plasmid-based vaccine for treating atherosclerosis. **Thomas, Lawrence J.** (T Cell Sciences, Inc., USA; Thomas, Lawrence J.). PCT Int. Appl. WO 9741227 A1 19971106, 66 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ,
DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US7294 19970501. PRIORITY: US 1996-640713 19960501; US 1997-802967 19970221.
AB A plasmid-based vaccine is provided that is based on the combination of DNA segments coding for one or more B cell epitopes of **CETP** and one or more broad range helper T cell epitopes. Administration of the plasmids as a vaccine to a vertebrate subject provides an immune response to the subject's endogenous **CETP** and modulation of **CETP** activity, leading to prevention or reversal of various manifestations of heart disease. The vaccines provide an advantageous strategy for the prevention or treatment of atherosclerosis.

L11 ANSWER 10 OF 12 SCISEARCH COPYRIGHT 2001 ISI (R)
97:166073 The Genuine Article (R) Number: WH142. A plasmid-based vaccine to elicit autoantibodies to cholesteryl ester transfer protein (**CETP**) for the prevention/treatment of atherosclerosis.. **Thomas L J (Reprint)**; Picard M D; Stewart S E; WAite B C D; Lin A Y; **Rittershaus C W**; Pettey C L. T CELL SCI INC, NEEDHAM, MA. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (JAN 1997) Vol. 99, No. 1, Part 2, Supp. [S], pp. 754-754. Publisher: MOSBY-YEAR BOOK INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318. ISSN: 0091-6749. Pub. country: USA
. Language: English.

L11 ANSWER 11 OF 12 BIOSIS COPYRIGHT 2001 BIOSIS
1997:144273 Document No.: PREV199799443476. A plasmid-based vaccine to elicit autoantibodies to cholesteryl ester transfer protein (**CETP**) for the prevention/treatment of atherosclerosis. **Thomas, L. J.**; Picard, M. D.; Stewart, S. E.; Waite, B. C. D.; Lin, A. Y.; **Rittershaus, C. W.**; Pettey, C. L.. T Cell Sci. Inc., Needham, MA USA. Journal of Allergy and Clinical Immunology, (1997) Vol. 99, No. 1 PART 2, pp. S187. Meeting Info.: Joint Meeting of the American Academy of Allergy, Asthma and Immunology, the American Association of Immunologists and the Clinical Immunology Society San Francisco, California, USA February 21-26, 1997 ISSN: 0091-6749. Language: English.

L11 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2001 ACS

1997:12606 Document No. 126:46315 Modulation of cholesteryl ester transfer protein (**CETP**) activity. **Rittershaus, Charles W.**; **Thomas, Lawrence J.** (T Cell Sciences, Inc., USA; Rittershaus, Charles W.; Thomas, Lawrence J.). PCT Int. Appl. WO 9634888 A1 19961107, 81 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US6147 19960501. PRIORITY: US 1995-432483 19950501.

AB This invention relates to peptides comprising a helper T cell epitope portion and a B cell epitope portion for eliciting an immune response against endogenous cholesteryl ester transfer protein (**CETP**) activity, to prevent or treat cardiovascular disease, such as atherosclerosis. The T helper T cell epitope may be derived from an antigenic peptide selected from the group consisting tetanus toxoid, diphtheria toxoid, pertussis vaccine, Bacile Calmette-Guerin, polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein deriv. of tuberculin, keyhole limpet hemocyanin, hsp70 and combination thereof.

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